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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/769,699	01/25/2001	Saul J. Silverstein	61152-A/JPW/AJM/HA	5342

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EXAMINER
LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 10/22/2002 12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/769,699	Applicant(s) SILVERSTEIN ET AL.	
	Examiner Gerald G Leffers Jr.	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *8,10 and 12-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-7, 9 and 11) in the response filed 7/15/02 Paper No. 11 is acknowledged. The traversal is on the ground(s) that the separate groups are not distinct because they are all related (i.e. all feature some aspect of p29) and because the examiner has not demonstrated a serious search burden for examination of all of the claims of the different groups. This is not found persuasive because of the following reasons.

While the inventions of Groups I-V may be considered "related" or dependent, the MPEP clearly indicates that it is proper to restrict between "related" inventions so long as they are distinct. MPEP 802.01 states:

> **The law has long been established that dependent inventions (frequently termed related inventions) such as used for illustration above may be properly divided if they are, in fact,"distinct" inventions, even though dependent.**

Applicants' response ignores the argumcnts made by the examiner in Paper No. 10, mailed 6/7/02, as to why the inventions of the different groups are distinct and as to why there is an undue search burden for the examiner to examine all of the claims together. For example, the fact that each of the groups has a different classification means that the search required for the different groups is not the same and is, therefore, burdensome.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-23 are pending in this application, with claims 8, 10 and 12-23 are withdrawn from consideration as being directed to nonelected inventions. Claims 1-7, 9 and 11 are under consideration.

Sequence Compliance

Acknowledgement is made of applicants' submission of a paper copy of the sequence listing, corresponding computer readable form of the sequence listing (CRF) and attorney's statement that the content of the two is the same. However, as this submission is after the filing date of the application, a statement from applicants' representative that the submission comprises no new matter is missing. Correction is required in order for applicants to be in sequence compliance.

37 C.F.R. §1.821(g) reads:

> **(g) If any of the requirements of paragraphs (b) through (f) of this section are not satisfied at the time of filing under 35 U.S.C. 111(a) or at the time of entering the national stage under 35 U.S.C. 371, applicant will be notified and given a period of time within which to comply with such requirements in order to prevent abandonment of the application. Any submission in reply to a requirement under this paragraph must be accompanied by a statement that the submission includes no new matter.**

Claim Objections

Claim 11 is objected to because of the following informalities: it is drawn towards a nonelected claim (i.e. claim 10). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 9 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Each of the claims is directed towards compositions comprising a Varicella-Zoster Virus (VZV) protein, 29p. The specification teaches that the term 29p encompasses any "naturally-occurring" variant of the protein (page 9, lines 16-20). The 29p protein described in the specification comprises 1,203 amino acid residues (SEQ ID NO: 2). The specification teaches that the compositions of the invention are useful for delivery of agents into a cell for the purposes of therapy, prophylaxis, diagnosis or cell labeling. Claims 1-4, 6-7, 9 and 11 specifically recite that the 29p protein mediates delivery of an agent to a target cell. The agent can literally be of "any physical category" (e.g. page 9, lines 21-26). The target cell can be literally any cell. Thus, each claim is drawn towards a potentially broad genus of variants of SEQ ID NO: 2 that must retain the ability to bind any agent (e.g. protein, nucleic acid, liposome, carbohydrate, metal composition, etc.) and deliver the agent into literally any target cell. Thus, the claimed invention embraces an enormously broad genus of combinations of 29p variant/bound agent/target cell receptor as a critical element of the invention.

The specification and prior art do not describe what are "naturally-occurring" variants of the 29p protein described in the specification (i.e. SEQ ID NO:2), much less which variants will retain the ability to simultaneous bind an agent and interact with a target cell such that the 29p/agent composition is delivered into the cell. For example, which domains of the protein are responsible for delivery of 29p to the cell interior? The specification describes experiments where it is shown that the protein described by SEQ ID NO: 2 can be secreted from certain cell types in vitro (e.g. human embryonic lung fibroblasts (HELF)) and that it can also enter certain

cells by endocytosis (e.g. cultured human neurons, human lymphocytes). The receptor or receptors responsible for delivery of the 29p protein into neuronal or lymphocytic cells are not described. No methods for the binding of agents (i.e. covalent or non-covalent binding) to 29p have been described by the instant specification, particularly with regard to maintaining the ability of 29p to be delivered into the cell interior via endocytosis. Therefore, the specification has not provided a structural/functional basis for one of skill in the art to envision a sufficient number of combinations of 29p variant/bound agent/target cell receptor to describe the broadly claimed genus of such combinations.

Delivery of agents into a particular target cell via linkage with 29p is a novel concept in the art and the prior art does not offset the deficiencies of the instant specification with regard to a structural/functional basis for one of skill in the art to envision combinations of 29p variant/bound agent/target cell receptor that function to deliver the agent into the target cell. Given the lack of a structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision those combinations of 29p variant/bound agent/target cell receptor that meet the functional limitations of the claims, one of skill in the would not be able to envision a sufficient number of specific embodiments to describe the broadly claimed genus of such combinations. Therefore, the skilled artisan would reasonably have concluded that applicants were not in possession of the claimed invention.

Claims 1-7, 9 and 11 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The invention is complex, involving the delivery of a desired compound into a desired target cell via the ability of a targeting protein to bind a receptor or receptors on the surface of the cell such that the compound is delivered into the interior of the cell. The desired agent is "bound" to the targeting protein by either covalent or non-covalent linkages (e.g. antibody binding) such that it is delivered along with the targeting protein.

Breadth of the claims: The breadth of the claims greatly exacerbates the complexity of the invention in that the claims are directed towards any target cell type and delivery of literally any agent not limited by any physical category. Thus, the claimed invention encompasses a huge combination of different compositions depending on different combinations of target cell type (i.e. receptor) and methods of binding the desired agent to the targeting protein, 29p. The claims are also broad in the sense that the specification teaches that the term "29p" includes any "naturally-occurring" variant of 29p.

Guidance of the specification/Working examples: The specification teaches that the VZF protein described by SEQ ID NO: 2 is secreted by human embryonic lung fibroblasts in vitro and can be taken in by endocytosis by neuronal or lymphocyte cells in vitro. SEQ ID NO: 2

describes a Varicella-Zoster Virus (VZV) protein that is 1,203 amino acids in length. The specification asserts that there are numerous teachings in the prior art of how to link different compounds (e.g. nucleic acids, proteins, etc.) to a protein. No such methods are actually taught in the specification. Those portions of the protein described by SEQ ID NO: 2 that are required for endocytosis are not taught by the specification. No "naturally-occurring" variants of SEQ ID NO: 2 are taught in the specification. The receptor or receptors involved in mediating 29p-based endocytosis are not taught in the specification. There are no working examples where a desired agent of any type is bound to 29p and delivered to a target cell of any type.

State of the art: Methods of detecting entry of a protein compound into a cell are known in the art. Methods of binding different compounds to a protein are known in the art. The concept of using 29p to deliver any agent into a target cell is novel in the prior art. Thus, the prior art does not provide teachings regarding those domains of 29p that can be modified by "binding" to any agent such that 29p and the agent will be delivered into a target cell. The prior art also does not identify which receptors on which cells might be capable of binding 29p and mediating endocytosis of 29p and any bound agent. Therefore, the prior art does not offset the deficiencies of the instant specification with regard to which combinations of 29p variant/agent/target receptor or receptors will work to deliver the agent to a desired cell.

Predictability of the art: Given the lack of teachings in the prior art as to what portions of SEQ ID NO: 2 can be modified by an agent such that it can be delivered, along with a desired agent, into a particular cell, and given the lack of teachings in the prior art as to what cell receptor or receptors are involved in 29p-mediated endocytosis, it would be unpredictable a priori as to which combinations of 29p variant/agent/cell receptor or receptors will function.

The amount of experimentation necessary: Given a full consideration of the factors listed above, particularly with regard to those factors that contribute to the unpredictability of the invention, it would take undue, unpredictable experimentation to make an use even one embodiment of the broadly claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 9 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7, 9 and 11 are vague and indefinite in that the metes and bounds of the term "29p" are unclear. The specification states the term "29p" encompasses "...protein having the sequence identified in Figure 6 or a naturally-occurring variant thereof" (page 9, lines 16-20). The specification and prior art do not clearly indicate what is a "naturally-occurring variant" of 29p. For example, which variants of 29p that are functional are also "naturally-occurring"? Therefore, the metes and bounds of the term are unclear. It would be remedial to explicitly recite that the protein is that described in Figure 6 (i.e. SEQ ID NO: 2).

Claims 1 and 7 recite a limitation concerning a "desired agent". The concept of a "desired" agent is highly subjective and is open to interpretation by each skilled artisan. It would be remedial to amend the claims by deleting the term "desired".

Claim 5 is vague and indefinite in that there is no clear and positive prior antecedent basis for the words "the protein". It would be remedial to amend the claim to read "the 29p protein".

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr.
Examiner
Art Unit 1636

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October 21, 2002